AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of identifying a ~~candidate~~ RAS-related C3 botulinum toxin substrate (RAC) pathway modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a Maternal Embryonic Leucine Zipper Kinase (MELK) polypeptide comprising SEQ ID NO: 6 or nucleic acid encoding SEQ ID NO: 6, wherein the assay system is capable of detecting the activity or expression of MELK;

(b) contacting the assay system with a test agent that modulates the activity or expression of MELK; and

(c) determining the activity or expression of the MELK polypeptide or nucleic acid in the assay system in the presence or absence of the test agent of step (b), wherein a change in MELK activity or expression between the presence and absence of the test agent identifies the test agent as a candidate RAC pathway modulating agent;

(d) providing a second assay system comprising cultured cells expressing MELK capable of detecting a change in the RAC pathway,

(e) contacting the second assay system with the test agent of step (b); and

(f) measuring the RAC pathway in the presence or absence of the test agent, wherein the detection of a difference in the presence and absence of the test agent confirms the test agent as a RAC pathway modulating agent.

2. (Original) The method of Claim 1 wherein the assay system comprises cultured cells that express the MELK polypeptide.

3. (Original) The method of Claim 2 wherein the cultured cells additionally have defective RAC function.

4. (Original) The method of Claim 1 wherein the assay system includes a screening

assay comprising a MELK polypeptide, and the candidate test agent is a small molecule modulator.

5. (Previously presented) The method of Claim 4 wherein the screening assay is a kinase assay.

6. (Original) The method of Claim 1 wherein the assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.

7. (Original) The method of Claim 1 wherein the assay system includes a binding assay comprising a MELK polypeptide and the candidate test agent is an antibody.

8. (Original) The method of Claim 1 wherein the assay system includes an expression assay comprising a MELK nucleic acid and the candidate test agent is a nucleic acid modulator.

9. (Original) The method of claim 8 wherein the nucleic acid modulator is an antisense oligomer.

10. (Previously presented) The method of Claim 8 wherein the nucleic acid modulator is a phosphothioate morpholino oligomer (PMO).

11. (Previously presented) The method of Claim 1 additionally comprising:

(d) administering the candidate RAC pathway modulating agent identified in (c) to a model system comprising cells defective in RAC function and detecting a phenotypic change in the model system that indicates that the RAC function is restored when compared relative to wild-type cells.

12. (Original) The method of Claim 11 wherein the model system is a mouse model with defective RAC function.

13. (Withdrawn) A method for modulating a RAC pathway of a cell comprising contacting a cell defective in RAC function with a candidate modulator that

specifically binds to a MELK polypeptide, whereby RAC function is restored.

14. (Withdrawn) The method of claim 13 wherein the candidate modulator is administered to a vertebrate animal predetermined to have a disease or disorder resulting from a defect in RAC function.

15. (Withdrawn) The method of Claim 13 wherein the candidate modulator is selected from the group consisting of an antibody and a small molecule.

16. -19. (Canceled)

20. (Withdrawn) A method of modulating RAC pathway in a mammalian cell comprising contacting the cell with an agent that specifically binds a MELK polypeptide or nucleic acid.

21. (Withdrawn) The method of Claim 20 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with the RAC pathway.

22. (Withdrawn) The method of Claim 20 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.

23. (Withdrawn) A method for diagnosing a disease in a patient comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the sample with a probe for MELK expression;

(c) comparing results from step (b) with a control;

(d) determining whether step (c) indicates a likelihood of disease.

24. (Withdrawn) The method of claim 23 wherein said disease is cancer.

25. (Withdrawn) The method according to claim 24, wherein said cancer is a cancer as shown in Table 1 as having >25% expression level.